Dietary magnesium intake can affect mechanical properties of rat carotid artery

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The purpose of the present study was to determine the effects of Mg deficiency and supplementation on the mechanical properties of the rat common carotid artery. The internal diameter and intra-arterial pressure of carotid artery were measured continuously using an echo-tracking device. Systolic, diastolic and mean intra-arterial pressures were not significantly different in Mg-deficient, -supplemented or control rats. Histological examination showed a larger cross-sectional area, increased intima-media thickness and a greater media:lumen value in carotid artery of Mg-deficient rats, indicating that Mg deficiency may directly stimulate growth and/or proliferation of arterial wall components. In addition, we observed a negative linear relationship between intima-media thickness and plasma Mg concentration, suggesting that increased Mg intake may counteract arterial wall hypertrophy. Neither Mg deficiency nor supplementation modified the arterial distensibility *v.* intra-arterial pressure curve or the E_{inc} *v.* wall stress curve, indicating that dietary Mg intake did not modify wall stiffness in young rats. At mean intra-arterial pressure, the stress and E_{inc} values were, however, significantly lower in Mg-deficient rats ($P < 0{\cdot}05$ in both cases); this finding could be related to the alteration in the geometry of the carotid artery. In conclusion, these findings suggest that Mg deficiency modifies the mechanical properties of the common carotid artery in young rats. Since Mg deficiency is considered a risk factor, these mechanical alterations could contribute to the development of atherosclerosis, hypertension and cardiovascular diseases.

Magnesium intake: Echo tracking: Wall thickness: Calcium

Mg in food represents the major portion of Mg intake in the general population. In developed countries, the recommended dietary allowances for Mg have been set at 4·5 mg/kg per d (Shils & Rude, 1996). It has been postulated, however, that a Mg intake of at least 6 mg/kg per d is needed to ensure adequate Mg status (Seelig, 1964; Marx & Neutra, 1997). Recent surveys of the food intake of individuals have revealed that a major portion of the population have dietary Mg intake lower than recommended dietary allowances (Shils & Rude, 1996; Galan *et al.* 1997; Marx & Neutra, 1997). Mg deficiency (defined as a reduction in total content of Mg in the body) due to an insufficient Mg intake can result in serious cardiovascular complications in human subjects and Mg deficiency is considered a risk factor for hypertension, IHD, congestive heart failure, acute myocardial infarction, cardiac arrhythmias and vascular complications in diabetes mellitus. Furthermore, several common clinical conditions such as diabetes mellitus, long-term treatment with thiazide diuretics, and chronic alcoholism causes Mg deficiency (Seelig, 1989; Karppanen, 1990; Eisenberg, 1992; Altura *et al.* 1993; Altura & Altura, 1995*a*,*b*). Some studies have demonstrated that Mg supplementation may be a protective factor against hypertension and cardiovascular diseases even when Mg deficiency has not been diagnosed or in cases of hypomagnesaemia (Dyckner & Wester, 1983; Woods *et al.* 1992; Itoh *et al.* 1997; Kawano *et al.* 1998). Other researchers do not agree (Cappucio *et al.* 1985; Zemel *et al.* 1990; Fourth International Study of Infarct Survival Collaborative Groups, 1995).

Cardiomyopathy and vascular lesions including wall thickening, endothelial and smooth muscle cell hyperplasia, inflammation of the media and the intima, and fibrinoid

Abbreviations: BP, blood pressure; CCA, common carotid artery; CSA, cross sectional area; E_{inc}, incremental elastic modulus; IAP, intra-arterial pressure; id, internal diameter; IMT, intima-media thickness.

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necrosis have been reported in small blood vessels of young animals fed a Mg-deficient diet (Bloom, 1985; Rayssiguier & Gueux, 1986). Experimental studies in rats, which can develop an atherosclerotic-like state, have indicated that dietary Mg deficiency elevates serum lipid concentrations, increases the susceptibility of lipoproteins to peroxidation (Rayssiguier & Gueux, 1986; Luthringer *et al.* 1988; Altura *et al.* 1990, 1993; Altura & Altura, 1995*b*), leading to inflammatory events, oxidation modifications of lipoproteins and free-radical damage that could play a significant role in atherogenesis and pathogenesis of vascular lesions (Rayssiguier *et al.* 1996; Shivakumar & Prakash Kumar, 1997). Clinically, an increase in intima-media thickness (IMT) of the carotid artery, measured by ultrasonography, is considered to reflect early artherosclerosis (Bonithon-Kopp *et al.* 1991; Heiss *et al.* 1991). An inverse relationship between serum Mg concentration and IMT of the human carotid artery has been demonstrated (Ma *et al.* 1995). These experimental and clinical findings support the importance of Mg deficiency in the pathogenesis of atherosclerosis, and suggest that Mg deficiency may also contribute to structural modifications of blood vessels, mainly arteries, that should alter their viscoelastic properties and thus, modify blood pressure (BP) level.

BP levels are closely correlated with vascular structure (Folkow, 1982). In rat, chronic Mg deficiency-induced hypertension is associated with structural modifications of mesenteric microvessels (decreased lumen diameter) (Altura *et al.* 1992). *In vitro* lowering of extracellular Mg concentration decreases lumen diameter and increases media thickness of rat mesenteric resistance arteries (Laurant *et al.* 1997). Although no studies are available on the mechanical properties of resistance arteries in chronic Mg-deficient state, these blood vessels have the capacity to adapt to increased wall stress by reorganizing the component of the media (remodelling) and/or by thickening the media (hypertrophy) in hypertension (Mulvany, 1999). Large arteries hardly contribute at all to peripheral resistance. Their buffering capacity contributes to the pulsatile component of blood pressure and they are a major determinant of cardiac afterload. Generally, the adaptation of conductance arteries to hypertension is associated with hypertrophy of the media and alteration in their visco-elasticity, i.e. increased passive stiffness and decreased compliance (Dobrin, 1983; Caputo *et al.* 1992). It is not yet known whether changes in dietary Mg intake contributes to modify elastic properties of the conductance arteries. The purpose of the present investigation was to study the effects of dietary Mg deficiency and supplementation on the structural and elastic properties of common carotid artery (CCA) in young rats.

Methods

Thirty Wistar male rats (3 weeks old) weighing 60 g (IFFA CREDO, L'Arbresle, France) were used. Animal care complied with applicable guidelines from the French Ministry of Agriculture. The rats were housed in plastic cages at a constant temperature of 23°C, constant humidity (50–60 %) and a daily 12 h light–dark cycle. They were randomly divided into Mg-deficient (80 mg/kg Mg), control (960 mg/kg Mg), and Mg-supplemented (6000 mg/kg Mg) groups. The rats were then pair-fed with the appropriate diets for 5 weeks. The synthetic diets contained (g/kg): casein 200, starch 400, sucrose 210, cellulose 60, groundnut oil 25, maize oil 25, mineral mixture 70, vitamin mixture 10. Mg was given in the form of MgO (Laurant *et al.* 1995)

BP was measured in non-anaesthetized restrained pre-warmed rats by the indirect tail-cuff method using a sphygmomanometer (PE-3000; Narco Biosystem, Houston, TX, USA). The lowest and the highest values were discarded before calculating the mean systolic BP of at least six clear readings.

On the day of the experiment, anaesthesia was induced and maintained with halothane at a concentration of 1·5 %. The right CCA was cannulated with a catheter (PE-50; Portex, London, UK) filled with heparinized NaCl (0·9 %, w/v) solution. Intra-arterial pressure (IAP) was monitored with a computerized data acquisition system. The internal diameter (ID) of the left CCA was measured at the same time with an A-mode ultrasonic echo-tracking device (NIUS-02; Asulab, Neuchatel, Switzerland) which has already been used and validated in human subjects and rats (Hayoz *et al.* 1992; Zanchi *et al.* 1997). The simultaneous arterial diameter and IAP measurements were processed on-line to calculate a diameter–pressure relationship, which was subsequently converted into an arterial cross-sectional distensibility *v.* pressure curve characterized over the whole range of operating BP.

At the end of the measurements, the animals were killed with a lethal dose (90 mg/kg intravenously) of pentobarbital. The left CCA was pressure-fixed in phosphate-buffered formaldehyde (4 %, v/v) and then excised and processed for histological examination as described previously (Zanchi *et al.* 1997). IMT and ID measurements were carried out with 200-fold magnification in a blinded procedure. The measurements carried out on two carotid sections and on six fields per section at a 60° angle were averaged. The intima-media cross-sectional area (CSA) of the fixed arteries was determined according to the formula: $CSA = \pi[(\text{internal radius} + IMT)^2 - (\text{internal radius})^2]$. The media:lumen value was calculated as $100 \times IMT/\text{internal radius}$. For estimation of incremental elastic modulus (E_{inc}) and mean circumferential stress (σ), arterial wall thickness was derived for each level of IAP from the CSA measured at histology and from the id measured *in vivo* (Zanchi *et al.* 1997). Wall thickness (h) was calculated according to the formula: $h = \sqrt{[(CSA + \pi(ID/2)^2)/\pi]} - ID/2$. Stress at each level of operational pressure (P) and ID was derived from the formula $\sigma = (P \times ID/2)/h$. E_{inc} was then defined as $E_{inc} = \Delta\sigma/\Delta\text{strain} = [\sigma_{(n+1)} - \sigma_n]/[ID_{(n+1)} - ID_n]$ and was calculated for each increase in intra-arterial BP of 2·5 mmHg within the operational IAP range.

Before artery fixation, blood samples were drawn from the right CCA of fasted rats and collected in heparinized tubes. Blood was immediately centrifuged at 2000 ***g*** for 15 min at 4°C. After appropriate dilution of the plasma, total Ca and Mg were analysed by atomic absorption spectrophotometry. Triacylglycerols and total cholesterol levels were determined by enzymatic methods (Boehringer Mannheim, Meylan, France).

Table 1. Body weight (BW), haemodynamic measurements and mechanical variables† for carotid arteries in anaesthetized control, magnesium deficient, and magnesium supplemented rats‡

(Values are means with their standard errors for eight rats per group)

	Control		Mg-deficient		Mg-supplemented	
	Mean	SE	Mean	SE	Mean	SE
BW (g)	274	4	255*	4	273	3
SIAP (mmHg)	128	2	122	2	128	4
DIAP (mmHg)	90	3	85	3	93	3
MIAP (mmHg)	103	3	98	2	105	3
PP (mmHg)	38	2	37	2	36	2
ID (μm)	965	64	921	35	1030	52
Dist (10^{-3}/mmHg)	8·16	0·42	8·58	0·43	7·74	0·56
Stress (N/cm^2)	3·52	0·12	2·76*	0·18	3·74	0·15
E_{inc} (N/cm^2)	7·36	0·94	4·91*	0·59	8·42	0·86

SIAP, systolic intra-arterial pressure; DIAP, diastolic intra-arterial pressure; MIAP, mean intra-arterial pressure; PP, pulse pressure; ID, internal diameter; Dist, distensibility; E_{inc}, incremental elastic modulus

Mean values were significantly different from those for control and Mg-supplemented rats: *$P < 0·05$.

† The mechanical variables (ID, Dist, stress, E_{inc}) were measured at mean blood pressure. Wall stress and E_{inc} were extrapolated and calculated on the basis of histomorphometric measurements, see p. 760.

‡ For details of diets and procedures, see p. 758.

Values are represented as means with their standard errors. Comparisons were performed using one-way ANOVA. A subsequent Student–Newman–Keul test was used to examine data for specific intergroup differences. The pressure *v.* ID, pressure *v.* distensibility, and wall stress *v.* E_{inc} curves were established within operating IAP. The curves were compared using ANOVA for repeated measures. Linear regression was analysed using Pearson correlation coefficients. Simultaneous independent effects of different variables on mechanical parameters were assessed by stepwise multivariate linear regression. $P < 0·05$ was considered statistically significant.

Results

Effect of dietary magnesium on blood pressure

During the experimental period, the Mg-deficient rats presented hyperaemia of the ears, alopecia and ulceration of the skin. Body weight increased with time, and Mg-deficient diet significantly decreased growth of the rats ($P < 0·05$). Mg supplementation had no effect on body weight (Table 1). BP measured in non-anaesthetized rats was similar for all three groups. When the rats were anaesthetized after 5 weeks of dietary treatment, systolic, diastolic, mean IAP, and pulse pressure of the control, Mg-deficient and Mg-supplemented rats were not significantly different (Table 1).

Effect of dietary magnesium on mechanical parameters of the common carotid artery

Mg deficiency and Mg supplementation did not affect the ID *v.* IAP curve when compared with the control treatment (Fig. 1). The ID values were significantly greater in CCA of Mg-supplemented rats than in Mg-deficient rats ($P < 0·05$). At mean IAP, ID of the CCA were similar for all three groups (Table 1). The increase in IAP significantly decreased arterial distensibility of the CCA from control, Mg-deficient and Mg-supplemented rats. Mg deficiency and Mg supplementation did not modify the arterial distensibility *v.* IAP curves (Fig. 1). At mean IAP, arterial distensibility was similar for Mg-deficient, Mg-supplemented and control rats (Table 1). Intergroup linear regression showed that distensibility was inversely related to systolic, diastolic and mean IAP (r −0·6009, r^2 0·3611, $P < 0·0051$) and confirmed the existing relationship between distensibility and IAP.

At mean IAP, wall stress was significantly less ($P < 0·05$) in CCA from Mg-deficient rats than in those from control and Mg-supplemented rats. Mg supplementation did not modify wall stress (Table 1). When E_{inc} *v.* wall stress was plotted the curves were not different for Mg-deficient, Mg-supplemented and control rats (Fig. 1). At mean IAP, E_{inc} was not significantly different between Mg-supplemented and control rats, but was significantly smaller ($P < 0·05$) in Mg-deficient rats (Table 1).

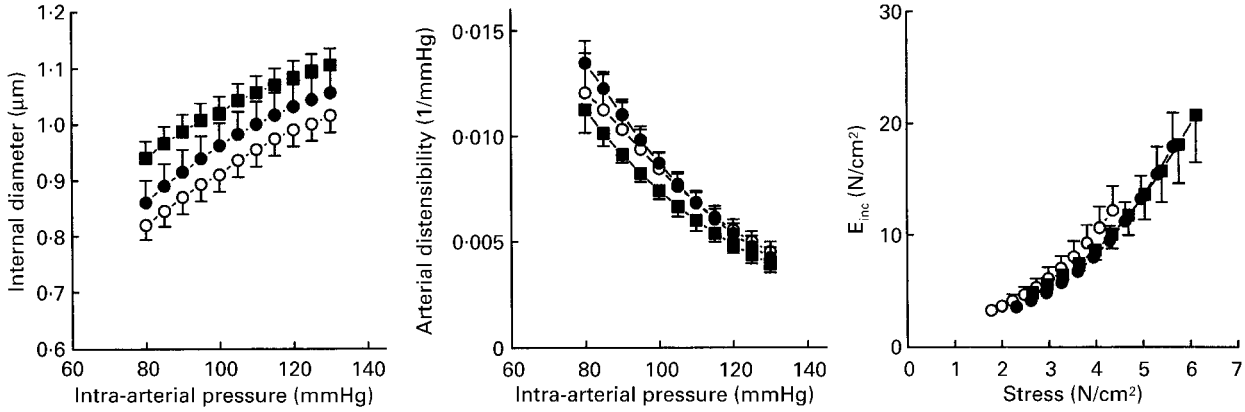

Fig. 1. Relationship between intra-arterial pressure and internal diameter, between intra-arterial pressure and arterial distensibility, and between circumferential wall stress and the incremental elastic modulus (E_{inc}) of the common carotid artery in Wistar rats fed control (●), magnesium-deficient (○) and magnesium-supplemented (■) diets. Data are means and their standard errors represented by vertical bars for seven to eight rats group. For details of diets and procedures, see p. 758.

Table 2. Histomorphometric characteristics of carotid arteries from control, magnesium-deficient and magnesium-supplemented rats†
(Values are means with their standard errors for eight rats per group)

	Control		Mg-deficient		Mg-supplemented	
	Mean	SE	Mean	SE	Mean	SE
IMT (μm)	22·2	0·8	27·2*	0·7	23·0	0·7
ED (μm)	601	11	615	19	611	14
CSA ($\times 10^3$ μm^2)	40·5	1·9	50·3*	2·3	42·6	2·0
M:L (%)	8·0	0·3	9·8*	0·3	8·1	0·2

IMT, intima-media thickness; ED, external diameter; CSA, cross-sectional area; M:L, media:lumen.
Mean values were significantly different from those for control and Mg-supplemented rats: *$P < 0·05$.
† For details of diets and procedures, see p. 758.

Effect of dietary magnesium on histomorphometric characteristics of the common carotid artery

The IMT, CSA and media:lumen of the fixed CCA artery were significantly greater ($P < 0·05$) in Mg-deficient rats. Mg deficiency did not affect the external diameter (Table 2). Mg supplementation did not significantly modify the histomorphometric variables of the CCA.

Effect of dietary magnesium on biochemical variables

In rats fed the Mg-deficient diet, the plasma total Mg concentration was significantly lower ($P < 0·01$), whereas total Ca and cholesterol concentrations were significantly higher ($P < 0·05$) than in the control rats (Table 3). In rats fed the Mg-supplemented diet, the plasma total Mg concentration was significantly higher ($P < 0·001$). Total Ca, cholesterol and triacylglycerol concentrations were not significantly modified. At mean IAP, plasma Mg concentration was inversely correlated with IMT (r −0·7567, r^2 0·5726, $P < 0·0001$), and positively correlated with ID (r 0·4567, r^2 0·2085, $P < 0·0374$), wall stress (r 0·8437, r^2 0·7119, $P < 0·0001$; Fig. 2), and E_{inc} (r 0·7573, r^2 0·5735, $P < 0·00011$; Fig. 3). At mean IAP, plasma Ca concentration was positively correlated with IMT (r 0·5101, r^2 0·2602, $P < 0·0182$) and inversely correlated with wall stress (r −0·5954, r^2 0·3545, $P<0·0072$; Fig. 2). No significant relationship was found between triacylglycerols or cholesterol and the mechanical variables studied.

Table 3. Biochemical variables obtained in plasma from control, magnesium-deficient, and magnesium-supplemented rats‡
(Values are means with their standard errors for eight rats per group)

	Control		Mg-deficient		Mg-supplemented	
	Mean	SE	Mean	SE	Mean	SE
Mg (mmol/l)	0·78	0·01	0·33**	0·05	0·97†	0·03
Ca (mmol/l)	2·69	0·01	2·89*	0·03	2·60	0·05
Chol (mmol/l)	1·65	0·05	1·87*	0·06	1·56	0·05
TAG (mmol/l)	1·13	0·11	1·14	0·06	1·06	0·12

Chol, cholesterol; TAG, triacylglycerols.
Mean values were significantly different from those for control and mg-supplement rats: *$P < 0·05$, **$P < 0·01$.
Mean values were significantly different from those for control rats: †$P < 0·001$.
‡ For details of diets and procedures, see p. 758.

Multiple regression analysis for IMT and wall stress showed that the effect of plasma Ca was no longer significant when added to plasma total Mg (IMT: r^2 0·578, $P = 0·0017$ for Mg, $P = 0·6461$ for Ca; wall stress: r^2 0·573, $P = 0·0004$ for Mg, $P = 0·4122$ for Ca), implying an interaction between Mg and Ca on IMT and wall stress.

Discussion

The aim of the present study was to evaluate the effect of dietary Mg intake on geometry, morphology and viscoelastic properties of the CCA of young rats. One of the main findings was that dietary Mg deficiency increases IMT of the arterial wall without affecting BP level. In contrast, dietary Mg supplementation had no significant effect, although we observed an intergroup negative linear relationship between plasma Mg level and IMT.

A recent epidemiological study has shown an inverse association between serum Mg and carotid wall thickness (Ma *et al.* 1995). The findings of the present experiment also confirm the deleterious effect of Mg deficiency on arterial wall thickness. In human subjects, thickening of the arterial wall of the carotid artery is considered to be an indicator of atherosclerosis (Bonithon-Kopp *et al.* 1991; Heiss *et al.* 1991). Experimental and clinical evidence suggest that alterations in lipid metabolism induced by Mg deficiency are linked to the development of atherosclerosis, and that dietary Mg intake plays an important modulatory role in controlling lipid metabolism in the arterial wall (Rayssiguier & Gueux, 1986; Altura *et al.* 1993). Mg deficiency increases triacylglycerols, total and free cholesterol concentrations, affects plasma lipoprotein distribution, enhances vascular lipid infiltration, increases oxygen-radical formation and increases susceptibility of lipoproteins to peroxidation (Luthringer *et al.* 1988; Altura *et al.* 1990; Altura & Altura, 1995*b*; Gueux *et al.* 1995; Lerma *et al.* 1995; Nassir *et al.* 1995; Rock *et al.* 1995). All or any one of these phenomena may be deleterious for the function, composition, and structure of blood vessels, causing atherogenesis and vascular diseases. On the other hand, oral Mg supplementation decreases plasma lipid concentration in human subjects and suppresses the development of atherosclerotic lesions in rodents (Rasmussen *et al.* 1989; Altura *et al.* 1990; Orimo & Ouchi, 1990; Saito *et al.* 1990). Experimental and clinical studies indicate that Mg supplementation has a beneficial effect on cardiovascular diseases (Dyckner & Wester, 1983; Cohen & Kitzes, 1984; Woods *et al.* 1992; Altura & Altura, 1995*a*,*b*; Lucas *et al.* 1995; Itoh *et al.* 1997; Kawano *et al.* 1998). In rat Mg supplementation attenuates development of genetic and mineralo-corticoid–salt hypertension, but has no effect on BP, heart function or vascular reactivity in normotensive rats (Berthelot & Esposito, 1983; Laurant *et al.* 1995). In the present study, it is not surprising, therefore, that Mg supplementation did not modify the structure or the mechanics of CCA in young normotensive rats. An interesting finding of our study was, however, the intergroup negative linear relationship between IMT of CCA and plasma total Mg; the higher the plasma Mg level, the lower the IMT. Together these findings suggest that

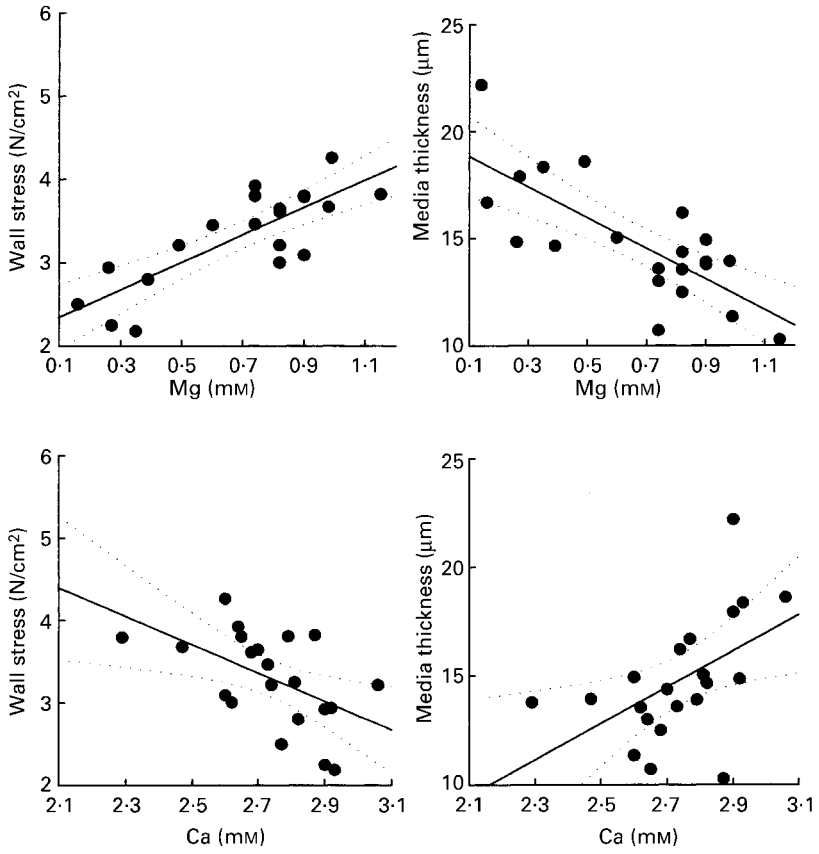

Fig. 2. Intergroup linear regression between internal diameter, intima-media thickness, circumferential wall stress and plasma magnesium and calcium concentrations within the groups of rats fed control, magnesium-deficient and magnesium-supplemented diets. For details of diets and procedures, see p. 758. At mean intra-arterial pressure, plasma magnesium concentrations were inversely correlated with intima-media thickness (r −0·7567, r^2 0·5726, $P < 0·0001$), and positively correlated with internal diameter (r 0·4567, r^2 0·2085, $P < 0·0374$), wall stress (r 0·8437, r^2 0·7119, $P < 0·001$). At mean intra-arterial pressure, plasma calcium concentration was positively correlated with intima-media thickness (r 0·5101, r^2 0·2602, $P < 0·0182$), and inversely correlated with wall stress (r −0·5954, r^2 0·3545, $P < 0·0072$).

increased Mg intake may play a protective role against arterial wall hypertrophy.

Generally, chronic elevation in BP, in both animals and human subjects, is characterized by increased arterial wall thickness. In rat short-term Mg deficiency does not change BP level. An initial transitory hypotensive phase has nevertheless been reported (Luthringer *et al.* 1988; Laurant *et al.* 1999*a*). Longer Mg-deficiency periods, however, markedly elevate BP levels and induce sustained hypertension (Altura *et al.* 1984, 1992; Laurant *et al.* 1999*a*,*b*). In the present study Mg deficiency did not change BP level but induced a larger CSA, increased IMT, a greater media:lumen value and a smaller ID of CCA, indicating both vascular remodelling and wall hypertrophy. In spontaneously-hypertensive rats arterial wall hypertrophy of the CCA precedes the development of hypertension, suggesting that change in the composition and/or the organization of the arterial wall might exist. This change may be related to factors other than BP *per se* (Zanchi *et al.* 1997). Our findings suggest that Mg deficiency may directly stimulate growth and/or proliferation of arterial wall constituents independently of BP elevation. Previous studies have shown that Mg deficiency induces morphological changes in arteries, such as hyperplasia and proliferation of endothelial and smooth muscle cells, calcification, fibrinoid necrosis and oedema with inflammatory infiltration (Britton & Stockstad, 1970; Bloom, 1985; Rayssiguier & Gueux, 1986). In rats Mg deficiency induces an inflammatory response, which may be involved in the pathogenesis of atherosclerosis. Mg deficiency increases the production of inflammatory and mitogenic factors such as cytokines, endothelin and platelet-derived growth factor by vascular smooth muscle and endothelial cells (Weglicki *et al.* 1992; Yokoyama *et al.* 1996). It has also been suggested that Mg deficiency plays a role in the production of other growth factors implicated in atherogenesis (Altura & Altura, 1995*b*). Recently, it has been shown that hypertriacylglycerolaemic serum from Mg-deficient rats stimulates cultured vascular smooth muscle cell proliferation, causes lipid accumulation in these cells and

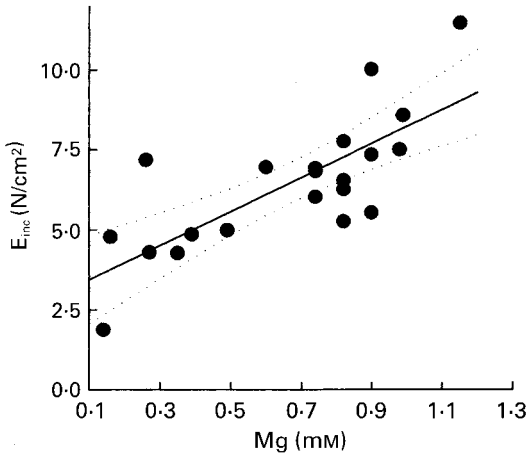

Fig. 3. Intergroup linear regression between incremental elastic modulus (E_{inc}) and plasma magnesium concentration within the groups of rats fed control, magnesium-deficient and magnesium-supplemented diets. For details of diets and procedures, see p. 758. At mean intra-arterial pressure, plasma magnesium concentration was positively correlated with E_{inc} (r 0·7573, r^2 0·5735, $P < 0·00011$).

lipoprotein oxidation in the arterial wall (Bussière *et al.* 1995). Although the cellular basis of the stimulatory effect of Mg deficiency on the development of atherosclerosis remains unclear, Ca might play a crucial role in the development of vascular atherosclerotic lesions (Altura *et al.* 1990; Orimo & Ouchi, 1990; Altura & Altura, 1995*b*). Ca stimulates growth of various cells and mediates migration, proliferation, matrix production and necrotization of vascular smooth muscle cells (Lichtman *et al.* 1983; Orimo & Ouchi, 1990; Fleckensteingrun, 1996). Extracellular Mg concentration influences Ca entry, binding, translocation and intracellular mobilization in vascular smooth muscle cells (Zhang *et al.* 1992; Altura *et al.* 1993). Hence, the decrease in extracellular Mg concentration, or hypomagnesaemia, results in an enhanced intracellular Ca level. Ca overloading in heart and blood vessels occurs as a general consequence of Mg deficiency (Rayssiguier & Gueux, 1986; Altura *et al.* 1992). The present study reported hypercalcaemia in Mg-deficient rats, and demonstrated, at mean BP, an intergroup positive linear relationship between IMT of CCA and plasma total Ca concentration. While the effect of Mg- and Ca-deficient or supplemented diets on vascular mechanical properties should be investigated, these findings strongly support the hypothesis that the elevation of circulating Ca levels induced by Mg deficiency (Rayssiguier & Gueux, 1986; Luthringer *et al.* 1988; Altura *et al.* 1990, 1993; Altura & Altura 1995*b*) may contribute to increased IMT of CCA of the rat.

One of the main functions of the conductance arteries is to buffer the pulsatile output from the heart and to provide a continuous flow to the distal vascular beds. The structural modifications induced by Mg deficiency are expected to modify the buffering function and the elastic properties of the wall (distensibility, E_{inc}) of the conductance arteries. Distensibility is dependent on the geometry of blood vessels and the stiffness of vascular wall components defined by E_{inc}. In Mg-deficient rats, as well as in Mg-supplemented rats, E_{inc} *v.* wall stress (which is recognized as being the best determinant of wall stiffness) was similar, at a given level of stress, to that of the control group. This finding indicates that the vascular wall intrinsic stiffness of Mg-deficient and Mg-supplemented rats is similar to that in control rats. At mean IAP the E_{inc} values were, however, lower in Mg-deficient than in control rats. In relation to BP the E_{inc} value is dependent on the geometry of the vessel wall, which affects wall stress. Interestingly, it was demonstrated that, at mean IAP, plasma Mg concentration is inversely related to IMT and positively related to wall stress and E_{inc}, suggesting that Mg may alter E_{inc} by altering vascular wall geometry. The intergroup positive linear relationship between plasma Mg level and E_{inc} value (the higher plasma the Mg concentration, the higher the E_{inc}) supports this hypothesis, since IMT decreased as the plasma Mg level increased. The physiological significance of these modifications is not clear since BP was not modified, particularly in Mg-deficient rats. Recently, we have shown that the hypertension induced by chronic dietary Mg deficiency in the rat is associated with an increase in arterial stiffness and an accelerated age-dependent decrease in distensibility of CCA (Laurant *et al.* 1999*b*), suggesting that the elevation of BP induced by long-term dietary Mg deficiency plays a role in altering visco-elastic properties of the vascular wall. Recent clinical reports have shown a positive linear relationship between aortic distensibility and intracellular free Mg concentration in hypertensive subjects, suggesting that intracellular Mg deficiency may contribute to arterial stiffness in hypertension (Resnick *et al.* 1997). Although the mechanisms involved in the stiffness of the vascular wall component are unclear, they could be related in part to differences in the composition, the characteristics and/or the organization of the structural components (more or less distensible) of the vascular wall. Several studies have shown that Mg deficiency may alter wall elasticity. Mg deficiency causes changes in the composition of blood vessels, such as calcification, increased collagen and decreased elastin content. Thinning, fragmentation of the elastic membranes and modification in synthesis, turnover and composition of elastin have also been reported (Rayssiguier & Gueux, 1986). In contrast, previous studies have shown that Mg supplementation improves vascular elasticity in patients suffering from arteriosclerosis (Niepper, 1974). The presence of Mg has been demonstrated in elastic fibres and it is speculated that the antagonism of Mg to Ca may protect the elastic fibre against Ca incorporation, thus playing a fundamental role in the maintenance of elasticity (Muller *et al.* 1993).

In conclusion, dietary Mg deficiency can alter CCA morphology in young rats, mainly in thickening and hypertrophy of the arterial wall; this change can contribute to the development of atherogenesis. These morphological alterations could modify the visco-elastic properties of conductance arteries. Since Mg deficiency is considered a risk factor, these mechanical alterations could contribute to the development of atherosclerosis, hypertension and cardiovascular complications.

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